Anaphylaxis To Oral Administration Of A PEG Laxative Product Confirmed With Oral Challenge

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Background

Polyethylene glycols (PEG) or macrogols are polymers widely used in drugs either as active substance (bowel preparations) or as excipients (antihistamines and corticosteroid injections among others), due to their wide range of physicochemical properties along with their safety profile (ubiquitous). Moreover, they can be found in additional medicinal (e.g. ultrasound gels) or hygiene products, cosmetics etc.

Sensitization is believed to occur from the latter (low molecular weight PEG easily penetrate the skin). Severe reactions though are reported with higher molecular weights (and doses) like in laxatives.

A variety of synonyms as well as insufficient labelling may contribute to the failure of suspecting the cause apart from the fact that often it is not the active substance (misdiagnosed then as "idiopathic" anaphylaxis).

Method

A 32yr caucasian woman presented with anaphylaxis (oral pruritus, hoarseness/ aphonia, palpitation, urticaria) immediately after receiving PO macrogol (13.3g of 3350MW) for constipation. She was treated with IV antihistamines & corticosteroids at an Emergency Dpt. 30′ later. The reaction subsided within 30′ and she fully recovered 6 hrs later.

Skin testings with the culprit commercial preparation were performed 12 weeks later (SPT undiluted, IDs 1/10,000, 1/1000, 1/100 dilutions). Quantification of specific IgE (ImmunoCAP®) and basophil activation test (BAT using CCR3+/CD63+ surface markers) were also performed. A single-blind placebo-controlled oral challenge was conducted to determine reaction threshold (1/1000, 1/100, 1/10, 1/3 and the remaining of the full recommended dose every 30′).

The authors state they have obtained patient's informed consent for presentation and publication of the present clinical case.

Results

All skin testings were negative. *However*, 30′ after the 1/100 dilution ID injection, the patient developed few urticarial wheals at distant sites along with mild hoarseness while ENT endoscopy showed mild edema of the arytenoids. Serum tryptase after 2 hrs was 4.7μg/L.

Specific IgE was negative, while BAT turned strongly positive (stimulation index 4.00).

Oral challenge was positive; an identical with the aforementioned after ID testing reaction occurred 30′ after the second dose (133mg).

Conclusion

Anaphylaxis was well documented based on the clinical history combined with the positive BAT and the observed reactions during skin testings and oral challenge.

However, an IgE mediated mechanism could not be proved, as skin testings and specific IgE were negative.

Considering that the patient uses skin products with PEG excipients without reaction, we could speculate that either the oral route of administration or higher doses or molecular weights are needed for anaphylaxis occurrence.

Discussion

Since 1990, approximately 40 patients (no children) have been reported (often to more than 1 drugs). In about 50%, laxatives were the offending agent and symptoms usually began immediately (almost instantly). Skin products never provoked anaphylaxis, but this observation does not apply for the mucosa nor a compromised epidermis.

Allergy work-up (special features): (1) skin testings should be evaluated in up to 30′ and ID dilutions should be considered to begin from as low as 0.0001% (2) specific IgE has never been detected in contrast to BAT or histamine release test which can turn positive.

Reference: Wenande E. et al, *Clin Exp Allergy* 46: 907-22, 2016